Interleukin-1 Receptor Antagonist-Like Proteins and Uses Thereof," which Applicants contend is clearly indicative of the invention to which the claims are directed.

2. Information Disclosure Statement

The Office Action states that Information Disclosure Statement filed March 26, 1997 fails to comply with the provisions of M.P.E.P. § 609 because an improper form PTO-1449 or equivalent was submitted. Specifically, the Action states that the EMBL database submission listed on the IDS fails to recite the name of the author and the date of publication. The Action also notes that the name of the author and the date of publication for this EMBL database submission has been added to the form PTO-1449, with the corrected document being made of record.

Applicants presume that the Information Disclosure Statement of which the Action refers is the Information Disclosure Statement filed June 21, 2001. Applicants thank the Examiner for correcting the form PTO-1449 by adding the author's name and publication date for the EMBL database submission listed on the IDS. Applicants believe that the corrected form PTO-1449 complies with the provisions of M.P.E.P. § 609, and note that the Action states that the corrected PTO-1449 has been made of record. However, Applicants would be happy to supply an updated copy of the Information Disclosure Statement, and would prefer to have the opportunity if the deficiencies in their previously-submitted Information Disclosure Statement will have the effect of leaving any of the cited references off the front page of any issued patent.

3. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 101

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 101. The Action states that the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Applicants traverse this rejection.

Applicants contend that the instant application contains an assertion of a specific and substantial utility for the claimed invention that would be credible to one of ordinary skill in the art. The instant application teaches a nucleotide sequence encoding an amino acid sequence for IL-1ra-L polypeptide (Figures 1A-1B). The instant application also teaches that IL-1ra-L polypeptide shares a high degree of amino acid sequence identity with two other members of the IL-1 family of proteins: IL-1δ (59% identity; 63% similarity) and IL-1ε (44% identity; 63% similarity) (Figure 2). In addition,

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the instant application teaches that IL-1ra-L polypeptide shares sequence identity with IL-1 β (31% identity; 45% similarity). With the exception of the amino acid sequence disclosed in GenBank Accession No. BAA84123 (phenol hydroxylase component), which shares the lowest degree of sequence identity with IL-1ra-L polypeptide, *all* of the related amino acid sequences identified in a BLAST search using the IL-1ra-L amino acid sequence (SEQ ID NO: 2) are members of the IL-1 family of proteins (Exhibit A; sequences that were publicly available at the time the instant application was filed are indicated in bold). Based on the expression of human IL-1ra-L mRNA in adult T cells, liver, lung, and spleen; placenta; and fetal kidney, scalp, and eye, as described at page 100, line 31 to page 111, line 4 and page 111, lines 10-11 of the specification, and the teaching that IL-1ra-L polypeptide shares homology with IL-1δ, IL-1ε, and IL-1 β, one of ordinary skill in the art would recognize that the claimed molecules could be useful, for example, in agonizing an IL-1 receptor in T cells, liver, lung, spleen, kidney, scalp, eye, or placenta.

Exhibit B illustrates that human IL-1ra-L polypeptide shares substantial amino acid sequence identity with a member of the IL-1 family disclosed by Smith *et al.*, 2000, *J. Biol. Chem.* 275:1169-75 (GenBank Accession No. AAF25213, published January 16, 2000; WO 00/71720, published November 30, 2000), and designated as IL-1 η. In addition, Smith *et al.* disclose that the IL-1 η gene possesses a conserved exon-intron structure shared by other members of the IL-1 family and that the IL-1 η gene is located on the long arm of chromosome 2 in a gene cluster with other members of the IL-1 gene family (Smith *et al.*, 2000, *J. Biol. Chem.* 275:1169-75). Applicants also note that because IL-1ra does not induce any intracellular response upon the binding of IL-1 receptor (Arend *et al.*, 1998, *Annu. Rev. Immunol.* 16:27-55), this molecule was designated as a member of the IL-1 family based solely on its amino acid sequence homology to IL-1 β and IL-1 α, similarities in gene structure, and common gene localization to human chromosome 2 (Arend, 1993, *Adv. Immunol.* 54: 167-227). Applicants contend that based on the totality of the evidence of record, one of ordinary skill in the art would recognize that IL-1ra-L polypeptide is a member of the IL-1 family of proteins. In fact, the Smith *et al.* reference cited above indicates that those of ordinary skill in the art, absent Applicants' teaching, *have* recognized that the polypeptide set forth in SEQ ID NO: 2 *is* a member of the IL-1 family of proteins, albeit subsequent to Applicants' identification of this member of the IL-1 family (indeed, after Applicants' priority filing date of December 10, 1999). Moreover, as members

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of the IL-1 family have substantial real world use, for example, as agonists or antagonists of inflammatory responses via binding to an interleukin receptor (Gabay, 2000, *Expert Opin. Investig. Drugs* 9:113-27), Applicants contend that one or ordinary skill in the art would recognize that the claimed molecules have credible, specific, and substantial utility.

Applicants contend that because the instant application contains an assertion of a specific and substantial utility for the claimed invention credible to one of ordinary skill in the art, the rejection under 35 U.S.C. § 101 should be withdrawn.

4. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that since the claimed invention is not supported by a specific and substantial asserted utility or a well-established utility, one skilled in the art would not know how to use the claimed invention.

Applicants have set forth affirmative evidence that the asserted utility would be credible to one of ordinary skill in the art. Applicants contend that because the instant application contains an assertion of a specific and substantial utility for the claimed invention that one of ordinary skill in the art would find to be credible, this rejection should be withdrawn.

The Office Action also asserts a rejection of claims 1, 2, 4-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that a deposit of biological material is necessary for the enablement of the claims because the specification does not provide a repeatable method for obtaining ATCC Deposit No. PTA-1215 and this deposit does not appear to be a readily available material. The Action also states that a deposit made in full compliance with 37 C.F.R. §§ 1.803-1.809 would satisfy the requirements of 35 U.S.C. § 112, first paragraph, provided that Applicants submit an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that a deposit has been made under the terms of the Budapest Treaty and that

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all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent.

Pursuant to the Examiner's request, Applicants submit herewith a Declaration stating that a deposit complying with 37 C.F.R. §§ 1.801-1.809 was made under the provisions of the Budapest Treaty. Applicants contend that all the requirements of 37 C.F.R. §§ 1.801-1.809 have been met. *In re Lundak,* 225 U.S.P.Q. 90 (Fed. Cir. 1985). Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 2-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that because the genus of IL-1ra-L variants recited in claims 2 and 3 is highly variant, and the specification fails to describe the common attributes or characteristics identifying the members of this genus, or provide a representative number of species to describe this genus, the Applicants were not in possession of the claimed genus of nucleic acid molecules at the time the application was filed.

Applicants have amended claim 2 to recite an isolated nucleic acid molecule comprising a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1215, encoding a polypeptide fragment of at least 25 amino acid residues; a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1215, comprising a fragment of at least 16 nucleotides; a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of either of these nucleic acid molecules; or a nucleotide sequence complementary to the nucleotide sequence of any of the above nucleic acid molecules. Applicants contend that because claim 2, as amended, recites only fragments of the disclosed human IL-1ra-L nucleic acid molecule (*i.e.*, SEQ ID NO: 1), one of ordinary skill in the art could readily determine the structure of nucleic acid molecules falling within the scope of this claim. Applicants therefore respectfully request that this ground of rejection be withdrawn.

Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2; a nucleotide sequence encoding a polypeptide as set

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forth in SEQ ID NO: 2 having a C- and/or N- terminal truncation, wherein the encoded polypeptide comprises at least 25 amino acid residues; a region of the nucleotide sequence of any of these nucleic acid molecules comprising a fragment of at least 16 nucleotides; a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of any of the above nucleic acid molecules; or a nucleotide sequence complementary to any of the above nucleic acid molecules. Applicants note that the instant application teaches the amino acid sequence for human IL-1ra-L polypeptide (Figures 1A-1B) and an amino acid sequence alignment (Figure 2) demonstrating that IL-1ra-L polypeptide shares a high degree of amino acid sequence identity with two other members of the IL-1 family of proteins: IL-1δ (59%) and IL-1ε (44%). The instant application also teaches that regions in IL-1ra-L polypeptide that are tolerable to conservative amino acid substitution can be identified by performing sequence comparisons between IL-1ra-L polypeptide and other related polypeptides (page 21, line 31 to page 22, line 13). The instant application further sets forth in Table I (page 21) rubrics recognized in the art for making conservative amino acid substitutions. In view of the teachings in the instant application, Applicants respectfully contend that one of ordinary skill in the art would understand the scope of species comprising the disclosed genus, and that the inventors were in possession of the invention having said scope at the time the application was filed. Thus, Applicants respectfully contend that their specification fulfills the requirements of 35 U.S.C. § 112, first paragraph, and request that this ground of rejection be withdrawn.

The Office Action also asserts a rejection of claims 2-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, because the specification while being enabling for a nucleic acid encoding a polypeptide as set forth in SEQ ID NO: 2, does not reasonably provide enablement for a nucleic acid encoding a polypeptide which is "at least about 70% identical to the polypeptide of SEQ ID NO: 2" or a nucleic acid molecule encoding a substitution, insertion, or deletion mutant of the polypeptide of SEQ ID NO: 2. The Action states that because the claims are overly broad, no guidance is provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid molecule encoding an IL-1ra-L polypeptide other than the one exemplified in the specification, and it is known in the art that even a single amino acid change in the amino acid sequence of a protein can have a dramatic effect on that protein's function, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

As described above, Applicants have amended claims 2 and 3 so that they no longer recite

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nucleic acid molecules comprising either a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in any of SEQ ID NO: 2; a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in any of SEQ ID NO: 1; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid insertion; or a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid deletion. Applicants contend that the claims, as amended, are not overly broad, and that in view of the specification's teachings, one of ordinary skill in the art could readily make and use the claimed nucleic acid molecules. Moreover, Applicants contend that while the references cited in the Action may teach that an amino acid change in the amino acid sequence of a protein can have a dramatic effect on that protein's function, these references do *not* teach that a *conservative* amino acid substitution would have this effect. Specifically, Mikayama *et al.*, 1993, *Proc. Natl. Acad. Sci.* U.S.A. 90:10056-60, teach that an asparagine-to-serine substitution at position 106 in human GIF destroys GIF function, and Voet *et al.*, *Biochemistry* 126-28, 228-34 (1990), teach that a glutamic acid-to-valine substitution in beta hemoglobin results in sickle-cell anemia. These are *not* "conservative substitutions" as that term is understood by those with skill in the art *or* as explicitly defined in the instant specification. Applicants note that the instant specification does not teach that an asparagine-to-serine substitution or a glutamic acid-to-valine substitution is either exemplary or preferred (Table I; page 22). Applicants contend that, in view of the specification's explicit teachings and knowledge in the art, it would not require undue experimentation for one of ordinary skill in the art to make and use the claimed invention, and therefore, Applicants respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

5. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as their invention.

The Action first asserts that claims 1-3 are indefinite for reciting the phrase "hybridizes under

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moderately or highly stringent conditions" because this phrase is relative and conditional. The Action states that some nucleic acids that might hybridize under conditions of moderate stringency would fail to hybridize under conditions of high stringency. Applicants note that the specification defines the meaning of the terms "moderately stringent conditions" (page 17, lines 12-18) and "highly stringent conditions" (page 16, lines 6-13), and provides examples of each. However, in order to more particularly point out and distinctly claim the subject matter that Applicants regard as their invention, Applicants have amended claims 1-3 to recite that the claimed nucleic acid molecules comprise a nucleotide sequence that "hybridizes under at least moderately stringent conditions." Applicants contend that the claims, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 2 is vague for reciting the phrase "about 70% identical" because the term "about" is inherently vague and indefinite. As discussed in section 3 above, Applicants have amended claim 2 so that it no longer recites a nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in any of SEQ ID NO: 2. In addition, Applicants have amended claim 2 to replace the term "at least about 25 amino acid residues" with the term "at least 25 amino acid residues," and claims 2 and 3 to replace the term "at least about 16 nucleotides" with the term "at least 16 nucleotides." Applicants contend that the claims, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 2 and 3 are vague and indefinite for reciting the phrase "has an activity of the polypeptide set forth in...SEQ ID NO: 2" because the activity of the polypeptide encoded by the nucleic acid being claimed is unclear. While Applicants respectfully disagree with the assertion that this phrase is indefinite, in an effort to expedite the present application to allowance Applicants have amended the pending claims to delete the phrase objected to in the Action, and affirmatively recite that C- and/or N- terminally truncated IL-1ra-L polypeptide variants must comprise at least 25 amino acid residues. Applicants contend that the claims, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 10 is vague and indefinite for reciting the phrase "other than the promoter DNA for the native IL-1ra-L polypeptide" because it is unclear which promoter DNA is being excluded and which is being included in the claim. Applicants have amended claim 10

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to recite that "the nucleic acid molecule comprises promoter DNA other than native IL-1ra-L promoter DNA." Applicants contend that because it is clear which promoter DNA is being excluded and which is being included, claim 10 is not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 46 is indefinite for reciting the term "fragment[s] thereof" because this term encompasses potentially any portion of the heterologous polypeptide including a single amino acid. Applicants have amended claim 46 to recite that the IgG constant domain fragment must be "biologically-active," and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 45 and 46, which are dependent upon non-elected claims 13, 14, or 15, should be amended to be dependent upon on elected nucleic acid claims, since the nucleic acid is utilized in production of the fusion proteins. Applicants have amended claims 45 and 46 to recite a nucleic acid molecule encoding a fusion polypeptide comprising the nucleic acid molecule of any of claims 1, 2, or 3 fused to DNA encoding a heterologous amino acid sequence. Because claims 45 and 46, as amended, are no longer dependent upon non-elected claims 13, 14, or 15, Applicants request that this ground of rejection be withdrawn.

The Action next asserts that claims 4-8, 11, and 42-44 are vague and indefinite for being dependent upon claims 1 and 2 for their limitations. Applicants contend that the claims, as amended, satisfy the requirements of 35 U.S.C. § 112, second paragraph, and therefore, respectfully contend that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

6. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 102

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 102(a), as being anticipated by International Publication No. WO 99/37662 (published July 29, 1999), contending that this reference discloses a nucleotide sequence of a cDNA molecule encoding a SPOIL protein, which would be capable of hybridizing under moderately stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1, or which, in the absence of an upper limit

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to the number of substitutions, deletions, or insertions, would meet the limitations of claim 3. Applicants traverse this rejection.

Applicants first note that the cDNA molecule disclosed in International Publication No. WO 99/37662 shares a sequence identity of 7.5% with the nucleotide sequence of SEQ ID NO: 1 (Exhibit C). In view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79% (page 17, lines 17-18), it is quite apparent that the cDNA molecule disclosed in WO 99/37662 would *not* hybridize to the nucleotide sequence of SEQ ID NO: 1 under Applicants' recited stringency conditions. In addition, as described in section 4 above, Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide *is at least 70 percent identical* to the polypeptide set forth in SEQ ID NO: 2. Applicants contend that claim 3, as amended, does not encompass the cDNA molecule disclosed in WO 99/37662. Applicants contend, therefore, that International Publication No. WO 99/37662 cannot anticipate the claims of the instant application, and respectfully request that this ground of rejection be withdrawn.

The Office Action next asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 102(b), as being anticipated by European Patent Application No. EP 0 855 404 (published July 29, 1998), contending that this reference discloses a nucleotide sequence of a cDNA molecule encoding an IL-1ra beta protein, which would be capable of hybridizing under moderately stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1, or which, in the absence of an upper limit to the number of substitutions, deletions, or insertions, would meet the limitations of claim 3. Applicants traverse this rejection.

Applicants first note that the cDNA molecule disclosed in European Patent Application No. EP 0 855 404 shares a sequence identity of 44.3% with the nucleotide sequence of SEQ ID NO: 1 (Exhibit D). As discussed above, in view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79%, it is quite apparent that the cDNA molecule disclosed in EP 0 855 404 would *not* hybridize to the nucleotide sequence of SEQ ID NO: 1 under Applicants' recited stringency conditions. In addition, as described in section 4 above, Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in

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SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide *is at least 70 percent identical* to the polypeptide set forth in SEQ ID NO: 2. Applicants contend that claim 3, as amended, does not encompass the cDNA molecule disclosed in EP 0 855 404. Applicants contend, therefore, that European Patent Application No. EP 0 855 404 cannot anticipate the claims of the instant application, and respectfully request that this ground of rejection be withdrawn.

The Office Action next asserts a rejection of claims 1-8, 10, and 42, under 35 U.S.C. § 102(b), as being anticipated by U.S. Patent No. 5,075,222 (issued December 24, 1991), contending that this reference discloses a nucleotide sequence of a cDNA molecule encoding an IL-1ra protein, which would be capable of hybridizing under moderately stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1, or which, in the absence of an upper limit to the number of substitutions, deletions, or insertions, would meet the limitations of claim 3. Applicants traverse this rejection.

Applicants first note that the cDNA molecule disclosed in U.S. Patent No. 5,075,222 shares a sequence identity of 24.4% with the nucleotide sequence of SEQ ID NO: 1 (Exhibit E). As discussed above, in view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79%, it is quite apparent that the cDNA molecule disclosed in U.S. 5,075,222 would *not* hybridize to the nucleotide sequence of SEQ ID NO: 1 under Applicants' recited stringency conditions. In addition, as described in section 4 above, Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide *is at least 70 percent identical* to the polypeptide set forth in SEQ ID NO: 2. Applicants contend that claim 3, as amended, does not encompass the cDNA molecule disclosed in U.S. 5,075,222. Applicants contend, therefore, that U.S. Patent No. 5,075,222 cannot anticipate the claims of the instant application, and respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 102 have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

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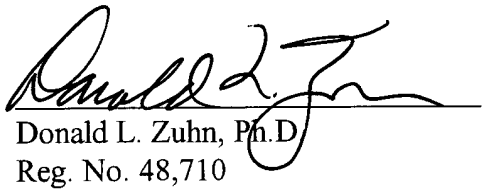
CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Mertz believes it to be helpful, she is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: January 16, 2003

By: 
Donald L. Zuhn, Ph.D.
Reg. No. 48,710

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 00-1214)

PATENT

In re Application of: **Welcher et al.**

Serial No.: **09/723,676**

Filed: **November 28, 2000**

For: **Interleukin-1 Receptor Antagonist-Like Molecules and Uses Thereof**

Before the Examiner: **P. Mertz**

Group Art Unit: **1646**

Commissioner for Patents
Washington, D.C. 20231

Sir:

DECLARATION

1. Applicants deposited cDNA encoding human IL-1ra-L polypeptide with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209.

2. The deposit was accepted by the ATCC, an International Depository Authority, under the provisions of the Budapest Treaty, and the deposit was designated as PTA-1215. A copy of the ATCC receipt for this deposit, showing the patent deposit designation (Accession No. PTA-1215) and the date on which the deposit was received by the ATCC (January 20, 2000) is attached.

3. Pursuant to 37 C.F.R. § 1.808(a)(2), the deposit was made under conditions that assure that all restrictions imposed by the depositors on the availability to the public of the deposited material would be irrevocably removed upon the granting of a patent relying on the deposited biological material.

4. In making the deposit, Applicants acknowledged their responsibility, pursuant to 37 C.F.R. § 1.805, to provide a replacement or supplemental deposit if the depository possessing the deposit is unable to furnish samples thereof or is able to furnish samples thereof but the deposit has become contaminated or has lost its capability to function as described in the specification.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: January 16, 2003

By: _____
Donald L. Zuhn, Ph.D.
Reg. No. 48,710

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ATCC

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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Amgen Inc.
Attn: Dawn Pohl
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

Deposited on Behalf of: Amgen Inc. (Ref. A-637-P)

Identification Reference by Depositor:	**Patent Deposit Designation**
Human IL-1ra like cDNA subcloned into the pGME-T easy Vector and transfected into DH10B bacteria	PTA-1215

The deposit was accompanied by: __ a scientific description X a proposed taxonomic description indicated above.

The deposit was received January 20, 2000 by this International Depository Authority and has been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested February 1, 2000. On that date, the culture was viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Barbara M. Hailey

Barbara M. Hailey, Administrator, Patent Depository

Date: February 1, 2000

cc: Scott N. Bernstein

EXHIBIT A

BLASTP 2.2.5 [Nov-16-2002]

Reference:
Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

RID: 1041959765-016166-6258

Query=
(157 letters)

Database: All non-redundant GenBank CDS translations+PDB+SwissProt+PIR+PRF
1,292,592 sequences; 412,925,052 total letters

Related Structures

Sequences producing significant alignments:	Score (bits)	E Value
gi|6694394|gb|AAF25213.1|AF201833_1 FIL1 eta [Homo sapiens]	**323**	**5e-88**
gi|20822718|ref|XP_130058.1| RIKEN cDNA 2310043N20 [Mus mus...	208	2e-53
gi|25008591|sp|Q9D6Z6|I1F8_MOUSE Interleukin 1 family membe...	206	6e-53
gi|20070252|ref|NP_055253.2| interleukin 1 family, member 8...	187	4e-47
gi|9665234|ref|NP_062564.1| interleukin 1 family, member 9;...	139	1e-32
gi|7657092|ref|NP_055255.1| interleukin 1 family, member 6 ...	139	1e-32
gi|20822740|ref|XP_130067.1| IL-1F9 [Mus musculus] >gi|2394...	137	4e-32
gi|9506601|ref|NP_062323.1| interleukin 1 family, member 9;...	116	9e-26
gi|19068184|gb|AAL67151.1| IL-1F7d [Homo sapiens]	89	2e-17
gi|10185738|gb|AAG14421.1|AF251119_1 interleukin-1-related ...	89	3e-17
gi|6694392|gb|AAF25212.1|AF201832_1 FIL1 zeta [Homo sapiens]	**89**	**3e-17**
gi|20127524|ref|NP_055254.2| interleukin 1 family, member 7...	89	3e-17
gi|25008597|sp|Q9QYY1|I1F5_MOUSE Interleukin 1 family membe...	79	2e-14
gi|9506807|ref|NP_062324.1| interleukin 1 family, member 5 ...	79	2e-14
gi|6912432|ref|NP_036407.1| interleukin 1 family, member 5 ...	78	4e-14
gi|23346487|ref|NP_694717.1| IL-1F10 [Mus musculus] >gi|250...	75	3e-13
gi|25008589|sp|Q8WWZ1|I1FA_HUMAN Interleukin 1 family membe...	74	5e-13
gi|20127669|ref|NP_115945.3| putatitve interleukin-1 recept...	74	6e-13
gi|124313|sp|P25085|IL1X_MOUSE Interleukin-1 receptor antag...	74	7e-13
gi|19068186|gb|AAL67154.1| IL-1F7e [Homo sapiens]	74	9e-13
gi|238585|gb|AAB20265.1| interleukin 1 receptor antagonist ...	**73**	**1e-12**
gi|13624317|ref|NP_112444.1| interleukin 1 receptor antagon...	73	1e-12
gi|10185740|gb|AAG14422.1| interleukin-1-related protein sh...	73	1e-12
gi|198390|gb|AAA39310.1| interleukin 1 receptor antagonist	**73**	**1e-12**
gi|12829966|gb|AAK01948.1| interleukin-1 receptor antagonis...	73	2e-12
gi|11559964|ref|NP_071530.1| interleukin 1 receptor antagon...	**72**	**4e-12**
gi|6166230|sp|O18999|IL1X_HORSE INTERLEUKIN-1 RECEPTOR ANTA...	**68**	**4e-11**
gi|3211711|gb|AAC39257.1| interleukin-1 receptor antagonist...	**68**	**5e-11**
gi|1274|emb|CAA38566.1| interleukin-1 beta [Ovis aries]	**68**	**5e-11**
gi|12746561|gb|AAK01472.1| interleukin-1 receptor antagonis...	**68**	**5e-11**
gi|124312|sp|P18510|IL1X_HUMAN Interleukin-1 receptor antag...	68	5e-11
gi|2997621|gb|AAC39672.1| interleukin-1 intracellular recep...	**67**	**6e-11**
gi|999512|pdb|1IRP| Interleukin-1 Receptor Antagonist Prot...	**67**	**6e-11**
gi|6016361|sp|Q29056|IL1X_PIG INTERLEUKIN-1 RECEPTOR ANTAGO...	**67**	**6e-11**
gi|69700|pir||ICBO1B interleukin-1 beta precursor - bovine ...	**67**	**6e-11**
gi|124314|sp|P26890|IL1X_RABIT INTERLEUKIN-1 RECEPTOR ANTAG...	**67**	**8e-11**
gi|7438656|pir||A39386 interleukin-1 receptor antagonist, 1...	**67**	**8e-11**
gi|10835147|ref|NP_000568.1| interleukin 1 receptor antagon...	67	9e-11

gi|6016360|sp|O77482|IL1X_BOVIN INTERLEUKIN-1 RECEPTOR ANTA...	**67**	**1e-10**
gi|996127|pdb|1ILR|2 Chain 2, Interleukin 1 Receptor Antago...	**67**	**1e-10**
gi|124307|sp|P21621|IL1B_SHEEP INTERLEUKIN-1 BETA PRECURSOR...	**66**	**1e-10**
gi|124302|sp|P09428|IL1B_BOVIN INTERLEUKIN-1 BETA PRECURSOR...	**65**	**3e-10**
gi|9836542|dbj|BAB11806.1| interleukin-1 receptor antagonis...	65	3e-10
gi|3211709|gb|AAC39256.1| interleukin-1 beta [Equus caballus]	**65**	**4e-10**
gi|6166229|sp|Q28386|IL1B_HORSE Interleukin-1 beta precurso...	64	6e-10
gi|11526781|gb|AAG36777.1|AF216526_1 interleukin-1 receptor...	64	8e-10
gi|7438655|pir||JC5646 interleukin-1 beta - horse >gi|24635...	**63**	**1e-09**
gi|124305|sp|P26889|IL1B_PIG INTERLEUKIN-1 BETA PRECURSOR (...	**63**	**1e-09**
gi|481234|pir||S38373 interleukin-1 beta precursor - pig >g...	**63**	**1e-09**
gi|17367201|sp|Q9WVG1|IL1B_CAVPO Interleukin-1 beta precurs...	63	2e-09
gi|1708445|sp|P51745|IL1B_CEREL Interleukin-1 beta precurso...	62	2e-09
gi|15489057|gb|AAH13644.1| Similar to replication initiatio...	62	2e-09
gi|6016358|sp|P79162|IL1B_CAPHI INTERLEUKIN-1 BETA PRECURSO...	**62**	**2e-09**
gi|3024024|sp|P79182|IL1B_MACFA INTERLEUKIN-1 BETA PRECURSO...	**61**	**5e-09**
gi|1352451|sp|P48090|IL1B_MACMU INTERLEUKIN-1 BETA PRECURSO...	**61**	**5e-09**
gi|1708446|sp|P51493|IL1B_MACNE INTERLEUKIN-1 BETA PRECURSO...	**61**	**5e-09**
gi|186288|gb|AAA59136.1| interleukin 1	**61**	**6e-09**
gi|18033002|gb|AAL56945.1|AF320322_1 interleukin-1 precurso...	61	6e-09
gi|15213526|gb|AAK92041.1|AF294754_1 interleukin-1 beta [Sa...	60	7e-09
gi|6680415|ref|NP_032387.1| interleukin 1 beta [Mus musculu...	60	7e-09
gi|26225025|gb|AAN76442.1| interleukin-1 beta precursor [Ma...	60	1e-08
gi|124306|sp|P14628|IL1B_RABIT INTERLEUKIN-1 BETA PRECURSOR...	**60**	**1e-08**
gi|494810|pdb|2MIB| Interleukin-1 Beta (Il-1 Beta) >gi|231...	**60**	**1e-08**
gi|1170531|sp|P41687|IL1B_FELCA INTERLEUKIN-1 BETA PRECURSO...	**60**	**1e-08**
gi|10835145|ref|NP_000567.1| interleukin 1, beta [Homo sapi...	59	2e-08
gi|124303|sp|P01584|IL1B_HUMAN Interleukin-1 beta precursor...	59	2e-08
gi|6520194|dbj|BAA87947.1| interleukin-1 beta [Tursiops tru...	**59**	**2e-08**
gi|208635|gb|AAA72561.1| interleukin 1-beta	**59**	**3e-08**
gi|494152|pdb|1HIB| Interleukin-1 Beta (Human) Mutant With...	**58**	**4e-08**
gi|26225027|gb|AAN76443.1| interleukin-1 beta precursor [Pa...	58	4e-08
gi|2905622|gb|AAC03536.1| interleukin 1 beta [Homo sapiens]	**58**	**4e-08**
gi|1827779|pdb|1IOB| Interleukin-1 Beta From Joint X-Ray A...	**58**	**5e-08**
gi|208637|gb|AAA72849.1| growth hormone:interleukin 1-beta ...	**58**	**5e-08**
gi|230947|pdb|41BI| Interleukin-1Beta (IL-1Beta) (Mutant W...	**58**	**5e-08**
gi|17367239|sp|Q9XS77|IL1B_TRIVU Interleukin-1 beta precurs...	58	5e-08
gi|1170530|sp|P46648|IL1B_CERTO INTERLEUKIN-1 BETA PRECURSO...	**57**	**6e-08**
gi|16417601|gb|AAL18817.1|AF421387_1 interleukin 1 beta pre...	57	1e-07
gi|13928692|ref|NP_113700.1| interleukin 1 beta [Rattus nor...	56	2e-07
gi|3175996|emb|CAA75239.1| interleukin-1beta [Gallus gallus...	55	3e-07
gi|230410|pdb|21BI| Interleukin-1Beta (IL-1Beta) (Mutant W...	**54**	**6e-07**
gi|230798|pdb|31BI| Interleukin-1Beta (IL-1Beta) (Mutant W...	**54**	**7e-07**
gi|5777787|emb|CAB53499.1| interleukin-1-beta [Xenopus laevis]	**49**	**2e-05**
gi|6468654|emb|CAB53541.3| interleukin-1 beta 2 precursor [...	48	5e-05
gi|25956174|emb|CAC33867.2| interleukin 1 beta protein [Sco...	48	5e-05
gi|3805826|emb|CAA06157.1| interleukin-1 beta [Oncorhynchus...	**47**	**7e-05**
gi|18152761|emb|CAC83518.1| interleukin-1 beta [Oncorhynchu...	47	8e-05
gi|2821975|dbj|BAA24538.1| interleukin-1 beta [Cyprinus car...	**47**	**1e-04**
gi|5708097|emb|CAB52366.1| interleukin-1-beta [Cyprinus car...	47	1e-04
gi|19911215|dbj|BAB86882.1| IL-1b [Paralichthys olivaceus]	45	4e-04
gi|3687837|gb|AAC62237.1| interleukin-1 receptor antagonist...	**45**	**5e-04**
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gi|12049719|emb|CAC19888.1| interleukin 1 beta 2-2 [Cyprinu...	41	0.005
gi|12049717|emb|CAC19887.1| interleukin 1 beta 2-1 [Cyprinu...	40	0.009
gi|14330417|emb|CAC41006.1| Interleukin-1 beta [Dicentrarch...	39	0.025
gi|25137092|emb|CAD12103.1| interleukin-1 beta-2 [Carassius...	36	0.20
gi|16945693|emb|CAD11603.1| interleukin-1 beta [Sparus aura...	33	1.1
gi|6016355|sp|P79161|IL1A_CAPHI INTERLEUKIN-1 ALPHA PRECURS...	**33**	**1.2**
gi|539767|pir||A61246 interleukin-1 alpha precursor - sheep	**32**	**2.3**
gi|3687909|gb|AAD04132.1| interleukin-1 receptor antagonist...	**32**	**3.6**
gi|5851794|dbj|BAA84123.1| phenol hydroxylase component [Ra...	**31**	**4.5**

EXHIBIT B

Aligned Length = 157 Gaps = 0
Identities = 157 (100%) Similarities = 0 (0%)

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AAF25213      1 MNPQREAAPKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRD  50
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IL-1ra-L    101 QKPFLFFHNKEGSTSVFQSVSYPGWFIATSTTSGQPIFLTKERGITNNTN 150
AAF25213    101 QKPFLFFHNKEGSTSVFQSVSYPGWFIATSTTSGQPIFLTKERGITNNTN 150
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EXHIBIT C

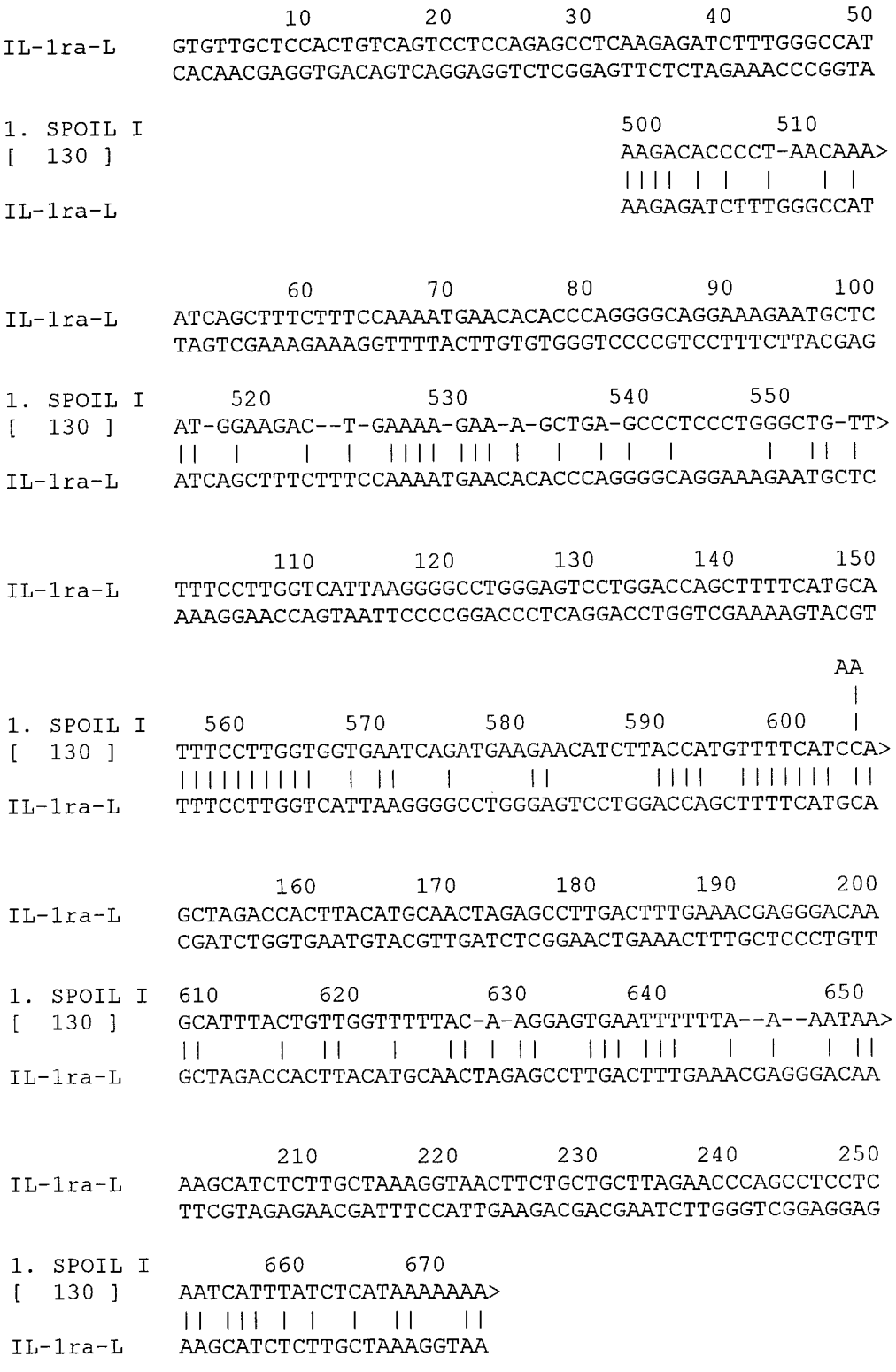
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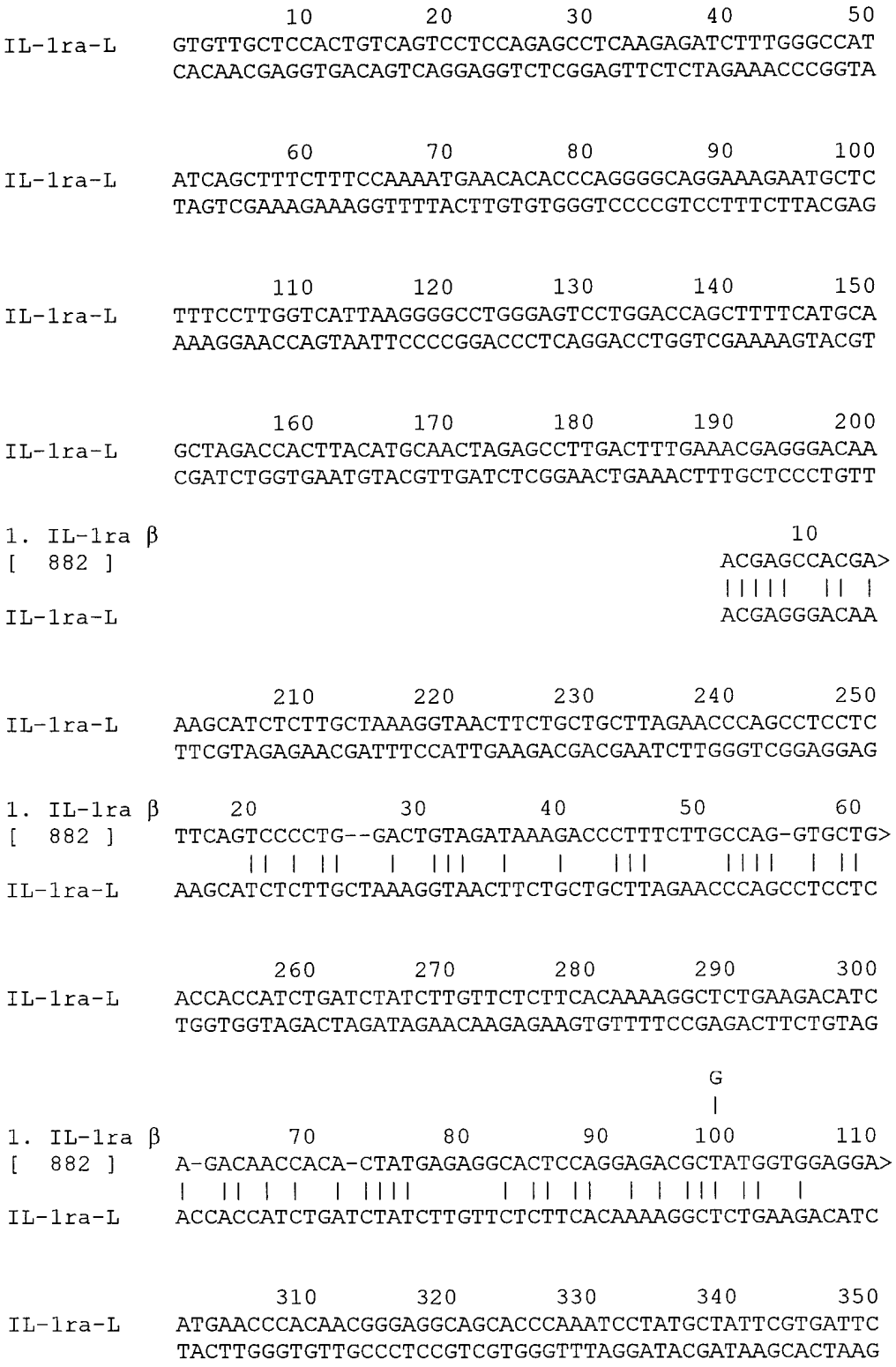
EXHIBIT D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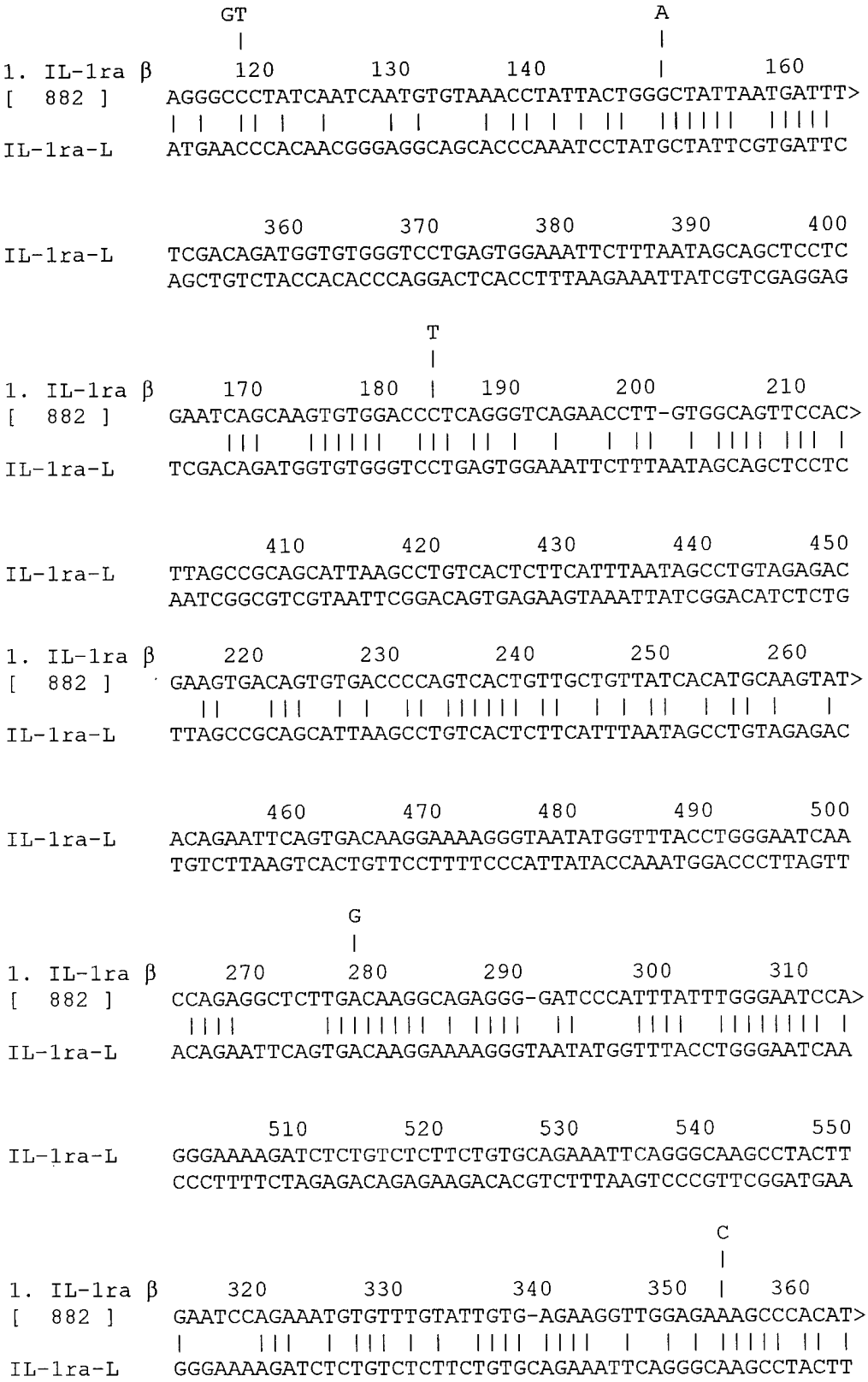
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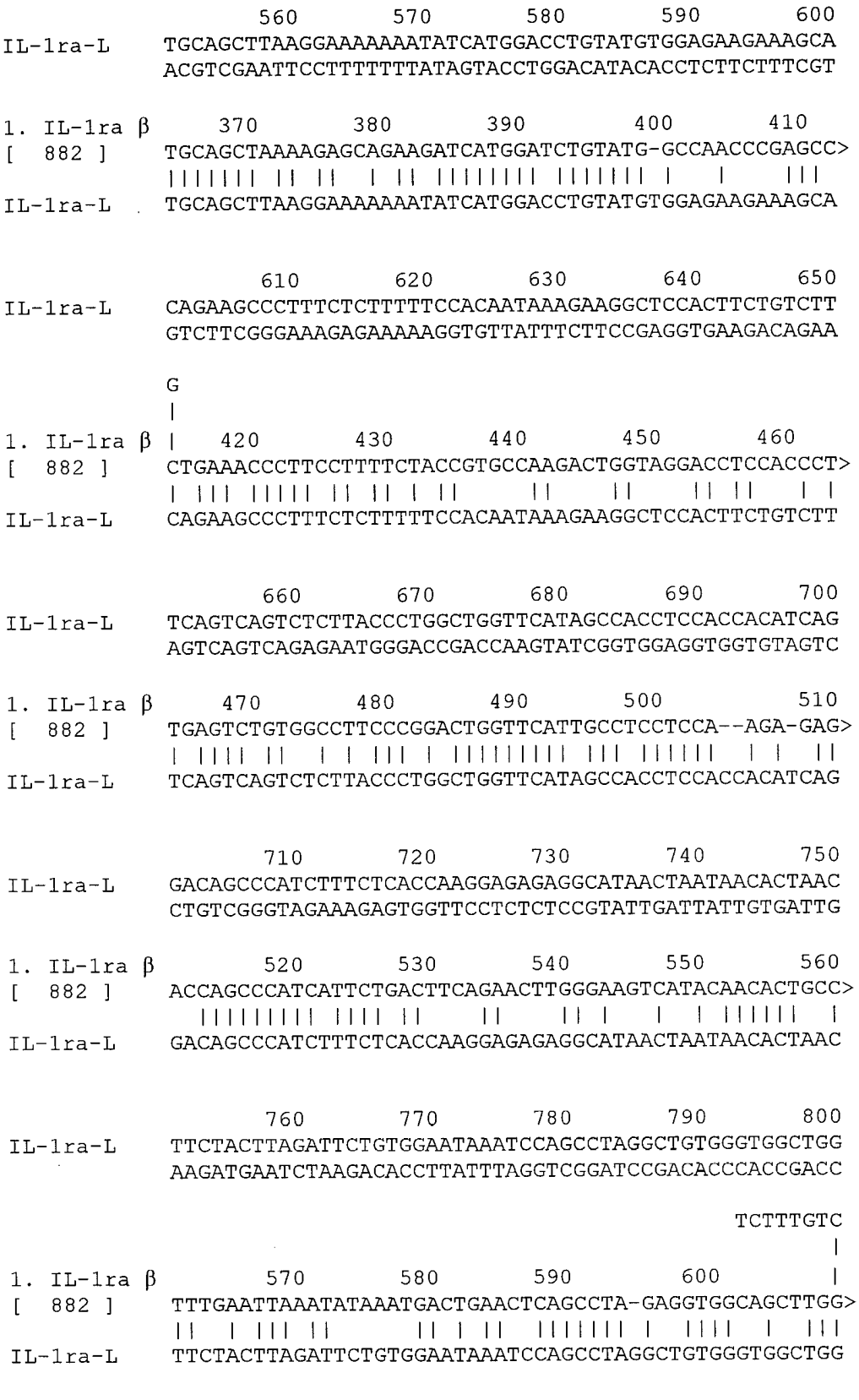
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IL-1ra-L GACAGCCCATCTTTCTCACCAAGGAGAGAGGCATAACTAATAACACTAAC
CTGTCGGGTAGAAAGAGTGGTTCCTCTCTCCGTATTGATTATTGTGATTG
1. IL-1ra β 520 530 540 550 560
[882] ACCAGCCCATCATTCTGACTTCAGAACTTGGGAAGTCATACAACACTGCC>
IL-1ra-L GACAGCCCATCTTTCTCACCAAGGAGAGAGGCATAACTAATAACACTAAC
760 770 780 790 800
IL-1ra-L TTCTACTTAGATTCTGTGGAATAAATCCAGCCTAGGCTGTGGGTGGCTGG
AAGATGAATCTAAGACACCTTATTTAGGTCGGATCCGACACCCACCGACC
TCTTTGTC
1. IL-1ra β 570 580 590 600
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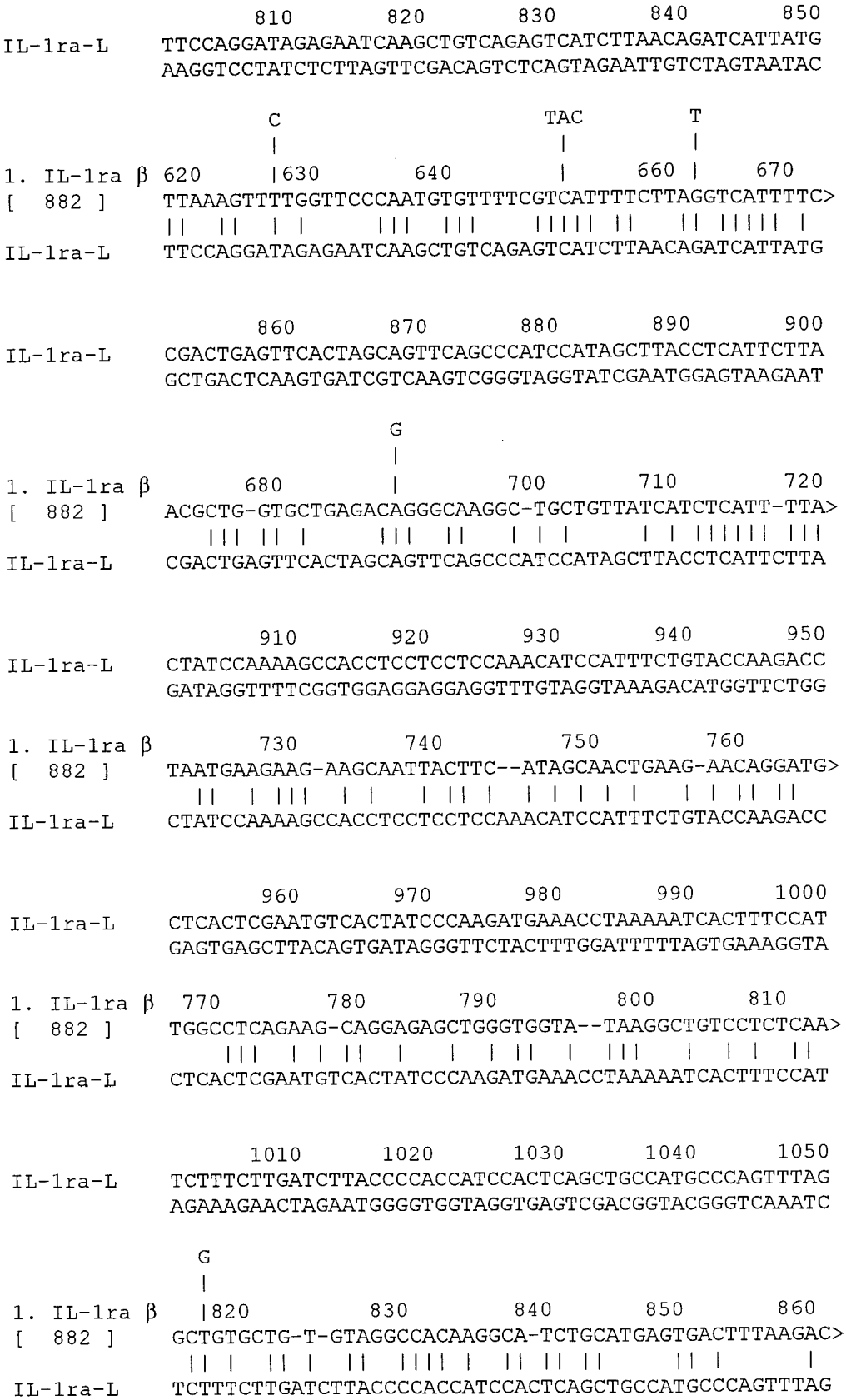
IL-1ra-L TTCTACTTAGATTCTGTGGAATAAATCCAGCCTAGGCTGTGGGTGGCTGG


810 820 830 840 850
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AAGGTCCTATCTCTTAGTTCGACAGTCTCAGTAGAATTGTCTAGTAATAC
C TAC T
1. IL-1ra β 620 630 640 660 670
[882] TTAAAGTTTTGGTTCCCAATGTGTTTTCGTCATTTTCTTAGGTCATTTTC>
IL-1ra-L TTCCAGGATAGAGAATCAAGCTGTCAGAGTCATCTTAACAGATCATTATG
860 870 880 890 900
IL-1ra-L CGACTGAGTTCACTAGCAGTTCAGCCCATCCATAGCTTACCTCATTCTTA
GCTGACTCAAGTGATCGTCAAGTCGGGTAGGTATCGAATGGAGTAAGAAT
G
1. IL-1ra β 680 700 710 720
[882] ACGCTG-GTGCTGAGACAGGGCAAGGC-TGCTGTTATCATCTCATT-TTA>
IL-1ra-L CGACTGAGTTCACTAGCAGTTCAGCCCATCCATAGCTTACCTCATTCTTA
910 920 930 940 950
IL-1ra-L CTATCCAAAAGCCACCTCCTCCTCCAAACATCCATTTCTGTACCAAGACC
GATAGGTTTTCGGTGGAGGAGGAGGTTTGTAGGTAAAGACATGGTTCTGG
1. IL-1ra β 730 740 750 760
[882] TAATGAAGAAG-AAGCAATTACTTC--ATAGCAACTGAAG-AACAGGATG>
IL-1ra-L CTATCCAAAAGCCACCTCCTCCTCCAAACATCCATTTCTGTACCAAGACC
960 970 980 990 1000
IL-1ra-L CTCACTCGAATGTCACTATCCCAAGATGAAACCTAAAAATCACTTTCCAT
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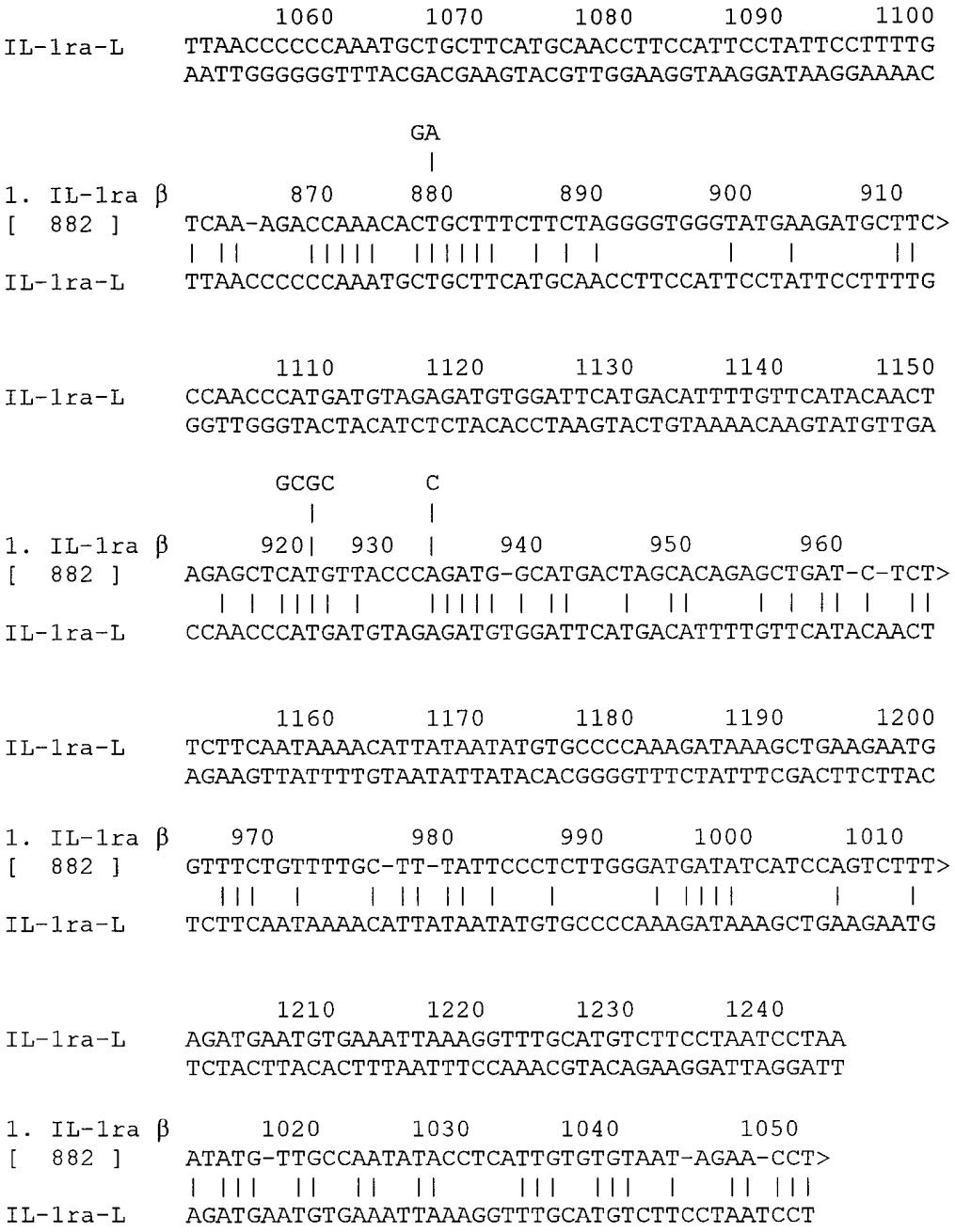
1. IL-1ra β 770 780 790 800 810
[882] TGGCCTCAGAAG-CAGGAGAGCTGGGTGGTA--TAAGGCTGTCCTCTCAA>
IL-1ra-L CTCACTCGAATGTCACTATCCCAAGATGAAACCTAAAAATCACTTTCCAT
1010 1020 1030 1040 1050
IL-1ra-L TCTTTCTTGATCTTACCCCACCATCCACTCAGCTGCCATGCCCAGTTTAG
AGAAAGAACTAGAATGGGGTGGTAGGTGAGTCGACGGTACGGGTCAAATC
G
1. IL-1ra β 820 830 840 850 860
[882] GCTGTGCTG-T-GTAGGCCACAAGGCA-TCTGCATGAGTGACTTTAAGAC>
IL-1ra-L TCTTTCTTGATCTTACCCCACCATCCACTCAGCTGCCATGCCCAGTTTAG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GA
1. IL-1ra β 870 880 890 900 910
[882] TCAA-AGACCAAACACTGCTTTCTTCTAGGGGTGGGTATGAAGATGCTTC>
IL-1ra-L TTAACCCCCCAAATGCTGCTTCATGCAACCTTCCATTCCTATTCCTTTTG
1110 1120 1130 1140 1150
IL-1ra-L CCAACCCATGATGTAGAGATGTGGATTCATGACATTTTGTTCATACAACT
GGTTGGGTACTACATCTCTACACCTAAGTACTGTAAAACAAGTATGTTGA
GCGC C
1. IL-1ra β 920 930 940 950 960
[882] AGAGCTCATGTTACCCAGATG-GCATGACTAGCACAGAGCTGAT-C-TCT>
IL-1ra-L CCAACCCATGATGTAGAGATGTGGATTCATGACATTTTGTTCATACAACT
1160 1170 1180 1190 1200
IL-1ra-L TCTTCAATAAAACATTATAATATGTGCCCCAAAGATAAAGCTGAAGAATG
AGAAGTTATTTTGTAATATTATACACGGGGTTTCTATTTCGACTTCTTAC
1. IL-1ra β 970 980 990 1000 1010
[882] GTTTCTGTTTTGC-TT-TATTCCCTCTTGGGATGATATCATCCAGTCTTT>
IL-1ra-L TCTTCAATAAAACATTATAATATGTGCCCCAAAGATAAAGCTGAAGAATG
1210 1220 1230 1240
IL-1ra-L AGATGAATGTGAAATTAAAGGTTTGCATGTCTTCCTAATCCTAA
TCTACTTACACTTTAATTTCCAAACGTACAGAAGGATTAGGATT
1. IL-1ra β 1020 1030 1040 1050
[882] ATATG-TTGCCAATATACCTCATTGTGTGTAAT-AGAA-CCT>
IL-1ra-L AGATGAATGTGAAATTAAAGGTTTGCATGTCTTCCTAATCCT

EXHIBIT E

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                    10         20         30         40         50
IL-1ra-L    GTGTTGCTCCACTGTCAGTCCTCCAGAGCCTCAAGAGATCTTTGGGCCAT
            CACAACGAGGTGACAGTCAGGAGGTCTCGGAGTTCTCTAGAAACCCGGTA

                    60         70         80         90        100
IL-1ra-L    ATCAGCTTTCTTTCCAAAATGAACACACCCAGGGGCAGGAAAGAATGCTC
            TAGTCGAAAGAAAGGTTTTACTTGTGTGGGTCCCCGTCCTTTCTTACGAG

                   110        120        130        140        150
IL-1ra-L    TTTCCTTGGTCATTAAGGGGCCTGGGAGTCCTGGACCAGCTTTTCATGCA
            AAAGGAACCAGTAATTCCCCGGACCCTCAGGACCTGGTCGAAAAGTACGT

                   160        170        180        190        200
IL-1ra-L    GCTAGACCACTTACATGCAACTAGAGCCTTGACTTTGAAACGAGGGACAA
            CGATCTGGTGAATGTACGTTGATCTCGGAACTGAAACTTTGCTCCCTGTT

                   210        220        230        240        250
IL-1ra-L    AAGCATCTCTTGCTAAAGGTAACTTCTGCTGCTTAGAACCCAGCCTCCTC
            TTCGTAGAGAACGATTTCCATTGAAGACGACGAATCTTGGGTCGGAGGAG

1. IL-1ra                                                     40
[  538 ]                                                CAGAGGCCTC>
                                                        |||   ||||
IL-1ra-L                                                CAGCCTCCTC

                   260        270        280        290        300
IL-1ra-L    ACCACCATCTGATCTATCTTGTTCTCTTCACAAAAGGCTCTGAAGACATC
            TGGTGGTAGACTAGATAGAACAAGAGAAGTGTTTTCCGAGACTTCTGTAG

1. IL-1ra       50         60         70         80         90
[  538 ]    CGCAGTCACCTA-ATCAC-TCTCCTCCTCTTCCTGTTCCATTCAGAGACG>
              ||    |  |  |  | | | ||| ||        |  |  ||| |
IL-1ra-L    ACCACCATCTGATCTATCTTGTTCTCTTCACAAAAGGCTCTGAAGACATC

                   310        320        330        340        350
IL-1ra-L    ATGAACCCACAACGGGAGGCAGCACCCAAATCCTATGCTATTCGTGATTC
            TACTTGGGTGTTGCCCTCCGTCGTGGGTTTAGGATACGATAAGCACTAAG

1. IL-1ra      100        110            120        130
[  538 ]    ATCTGCCCAC--CCTCTGGGAG-A---AAATCC-A-GCAAGATGCAAGCC>
            ||   |||||  |    || || |   |||||| | || |   |  |  |
IL-1ra-L    ATGAACCCACAACGGGAGGCAGCACCCAAATCCTATGCTATTCGTGATTC
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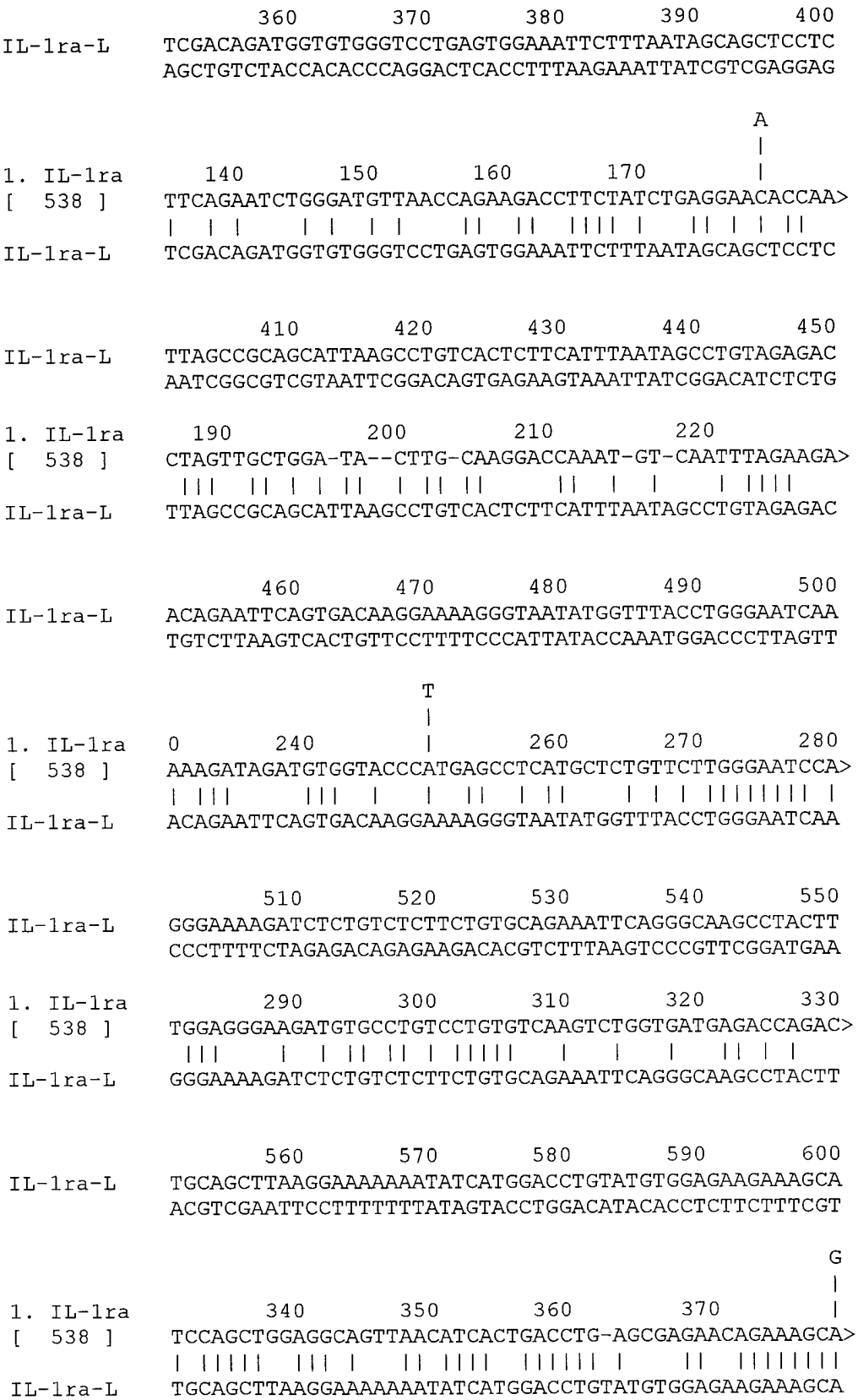
360 370 380 390 400
IL-1ra-L TCGACAGATGGTGTGGGTCCTGAGTGGAAATTCTTTAATAGCAGCTCCTC
AGCTGTCTACCACACCCAGGACTCACCTTTAAGAAATTATCGTCGAGGAG
A
1. IL-1ra 140 150 160 170
[538] TTCAGAATCTGGGATGTTAACCAGAAGACCTTCTATCTGAGGAACACCAA>
IL-1ra-L TCGACAGATGGTGTGGGTCCTGAGTGGAAATTCTTTAATAGCAGCTCCTC
410 420 430 440 450
IL-1ra-L TTAGCCGCAGCATTAAGCCTGTCACTCTTCATTTAATAGCCTGTAGAGAC
AATCGGCGTCGTAATTCGGACAGTGAGAAGTAAATTATCGGACATCTCTG
1. IL-1ra 190 200 210 220
[538] CTAGTTGCTGGA-TA--CTTG-CAAGGACCAAAT-GT-CAATTTAGAAGA>
IL-1ra-L TTAGCCGCAGCATTAAGCCTGTCACTCTTCATTTAATAGCCTGTAGAGAC
460 470 480 490 500
IL-1ra-L ACAGAATTCAGTGACAAGGAAAAGGGTAATATGGTTTACCTGGGAATCAA
TGTCTTAAGTCACTGTTCCTTTTCCCATTATACCAAATGGACCCTTAGTT
T
1. IL-1ra 0 240 260 270 280
[538] AAAGATAGATGTGGTACCCATGAGCCTCATGCTCTGTTCTTGGGAATCCA>
IL-1ra-L ACAGAATTCAGTGACAAGGAAAAGGGTAATATGGTTTACCTGGGAATCAA
510 520 530 540 550
IL-1ra-L GGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCCTACTT
CCCTTTTCTAGAGACAGAGAAGACACGTCTTTAAGTCCCGTTCGGATGAA
1. IL-1ra 290 300 310 320 330
[538] TGGAGGGAAGATGTGCCTGTCCTGTGTCAAGTCTGGTGATGAGACCAGAC>
IL-1ra-L GGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCCTACTT
560 570 580 590 600
IL-1ra-L TGCAGCTTAAGGAAAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCA
ACGTCGAATTCCTTTTTTTATAGTACCTGGACATACACCTCTTCTTTCGT
G
1. IL-1ra 340 350 360 370
[538] TCCAGCTGGAGGCAGTTAACATCACTGACCTG-AGCGAGAACAGAAAGCA>
IL-1ra-L TGCAGCTTAAGGAAAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCA

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                    610        620        630        640        650
IL-1ra-L    CAGAAGCCCTTTCTCTTTTTCCACAATAAAGAAGGCTCCACTTCTGTCTT
            GTCTTCGGGAAAGAGAAAAAGGTGTTATTTCTTCCGAGGTGAAGACAGAA

                                       T
                                       |
1. IL-1ra           390        400     |  410        420        430
[  538 ]    GACAAGCGCTTCGCCTTCATCCGCCAGACAG-TGGCCCCACCACCAGTTT>
             | |||| |||    |||  |||  | | | ||  |||  ||||  |     ||
IL-1ra-L    CAGAAGCCCTTTCTCTTTTTCCACAATAAAGAAGGCTCCACTTCTGTCTT

                    660        670        680        690        700
IL-1ra-L    TCAGTCAGTCTCTTACCCTGGCTGGTTCATAGCCACCTCCACCACATCAG
            AGTCAGTCAGAGAATGGGACCGACCAAGTATCGGTGGAGGTGGTGTAGTC

1. IL-1ra           440        450        460        470        480
[  538 ]    TGAGTCTGCCGCCTGCCCCGGTTGGTTCCTCTGCACAGCGATGGAAGCTG>
            | |||| | | | | ||| || |||||| |   |||  | |    | | |
IL-1ra-L    TCAGTCAGTCTCTTACCCTGGCTGGTTCATAGCCACCTCCACCACATCAG

                    710        720        730        740        750
IL-1ra-L    GACAGCCCATCTTTCTCACCAAGGAGAGAGGCATAACTAATAACACTAAC
            CTGTCGGGTAGAAAGAGTGGTTCCTCTCTCCGTATTGATTATTGTGATTG

                                TATGCC
                                  |
1. IL-1ra           490        500 510        520          530
[  538 ]    ACCAGCCCGTCAGCCTCACCAATGACGAAGGCGTCA-TGGT--CACCAAA>
              |||||| ||   |||||||| ||  |||| | | |  |  ||| ||
IL-1ra-L    GACAGCCCATCTTTCTCACCAAGGAGAGAGGCATAACTAATAACACTAAC

                    760        770        780        790        800
IL-1ra-L    TTCTACTTAGATTCTGTGGAATAAATCCAGCCTAGGCTGTGGGTGGCTGG
            AAGATGAATCTAAGACACCTTATTTAGGTCGGATCCGACACCCACCGACC

1. IL-1ra       540        550        560        570        580
[  538 ]    TTCTACTTCCAGGAGGACGAGT-AGTACTGCCCAGGC-CT-GCTGTTCCA>
            ||||||||  |    |  || | | | | ||| ||||  | | ||
IL-1ra-L    TTCTACTTAGATTCTGTGGAATAAATCCAGCCTAGGCTGTGGGTGGCTGG

                    810        820        830        840        850
IL-1ra-L    TTCCAGGATAGAGAATCAAGCTGTCAGAGTCATCTTAACAGATCATTATG
            AAGGTCCTATCTCTTAGTTCGACAGTCTCAGTAGAATTGTCTAGTAATAC

1. IL-1ra        590
[  538 ]    TTCTTGCAT-GGCAA>
            |||  | || |  ||
IL-1ra-L    TTCCAGGATAGAGAA

                    860        870        880        890        900
IL-1ra-L    CGACTGAGTTCACTAGCAGTTCAGCCCATCCATAGCTTACCTCATTCTTA
            GCTGACTCAAGTGATCGTCAAGTCGGGTAGGTATCGAATGGAGTAAGAAT
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                910        920        930        940        950
IL-1ra-L    CTATCCAAAAGCCACCTCCTCCTCCAAACATCCATTTCTGTACCAAGACC
            GATAGGTTTTCGGTGGAGGAGGAGGTTTGTAGGTAAAGACATGGTTCTGG

               960        970        980        990       1000
IL-1ra-L    CTCACTCGAATGTCACTATCCCAAGATGAAACCTAAAAATCACTTTCCAT
            GAGTGAGCTTACAGTGATAGGGTTCTACTTTGGATTTTTAGTGAAAGGTA

              1010       1020       1030       1040       1050
IL-1ra-L    TCTTTCTTGATCTTACCCCACCATCCACTCAGCTGCCATGCCCAGTTTAG
            AGAAAGAACTAGAATGGGGTGGTAGGTGAGTCGACGGTACGGGTCAAATC

              1060       1070       1080       1090       1100
IL-1ra-L    TTAACCCCCCAAATGCTGCTTCATGCAACCTTCCATTCCTATTCCTTTTG
            AATTGGGGGGTTTACGACGAAGTACGTTGGAAGGTAAGGATAAGGAAAAC

              1110       1120       1130       1140       1150
IL-1ra-L    CCAACCCATGATGTAGAGATGTGGATTCATGACATTTTGTTCATACAACT
            GGTTGGGTACTACATCTCTACACCTAAGTACTGTAAAACAAGTATGTTGA

              1160       1170       1180       1190       1200
IL-1ra-L    TCTTCAATAAAACATTATAATATGTGCCCCAAAGATAAAGCTGAAGAATG
            AGAAGTTATTTTGTAATATTATACACGGGGTTTCTATTTCGACTTCTTAC

              1210       1220       1230       1240
IL-1ra-L    AGATGAATGTGAAATTAAAGGTTTGCATGTCTTCCTAATCCTAA
            TCTACTTACACTTTAATTTCCAAACGTACAGAAGGATTAGGATT
```

AMENDMENTS TO THE SPECIFICATION

Marked Up Version of Replacement Paragraphs of Specification

under 37 C.F.R. 1.121(b)(1)(iii)

Please amend the title at page 1, lines 1-2 to read as follows:

NUCLEIC ACIDS ENCODING INTERLEUKIN-1 RECEPTOR ANTAGONIST-LIKE ~~MOLECULES~~ PROTEINS AND USES THEREOF

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AMENDMENTS TO THE CLAIMS

Marked Up Versions of Amended Claims under 37 C.F.R. 1.121(c)(1)(ii)

1. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence ~~selected from the group consisting of~~:

(a) ~~the nucleotide sequence~~ as set forth in SEQ ID NO: 1;

(b) ~~the nucleotide sequence~~ of the DNA insert in ATCC Deposit No. PTA-1215;

(c) ~~a nucleotide sequence~~ encoding ~~the~~ a polypeptide as set forth in SEQ ID NO: 2;

(d) ~~a nucleotide sequence which~~that hybridizes under at least moderately ~~or highly~~ stringent conditions to the complement of the nucleotide sequence of any of (a) - (c); ~~and~~ or

(e) ~~a nucleotide sequence~~ complementary to the nucleotide sequence of any of (a) - ~~(e)~~(d).

2. (Amended) An isolated nucleic acid molecule comprising ~~a nucleotide sequence selected from the group consisting of~~:

~~(a) a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in SEQ ID NO: 2, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2;~~

~~(b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in SEQ ID NO: 1, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1215, or (a);~~

~~(c)~~(a) a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1215, ~~(a), or (b)~~ encoding a polypeptide fragment of at least ~~about~~ 25 amino acid residues~~, wherein the polypeptide fragment has an activity of the encoded polypeptide as set forth in SEQ ID NO: 2, or is antigenic~~;

~~(d)~~(b) a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1215, ~~or any of (a) - (c)~~ comprising a fragment of at least ~~about~~ 16 nucleotides;

~~(e)~~(c) a nucleotide sequence ~~which~~ that hybridizes under at least moderately ~~or highly~~ stringent conditions to the complement of the nucleotide sequence of either ~~any of~~ (a) ~~- (d)~~ or (b); ~~and~~ or

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~~(f)~~(d) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - ~~(d)~~(c).

3. (Amended) An isolated nucleic acid molecule comprising ~~a nucleotide sequence selected from the group consisting of~~:

(a) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide ~~has an activity of~~ is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2;

~~(b) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2;~~

~~(c) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid deletion, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2;~~

~~(d)~~(b) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 ~~which~~ hasving a C- and/or N- terminal truncation, wherein the encoded polypeptide ~~has an activity of the polypeptide set forth in SEQ ID NO: 2~~ comprises at least 25 amino acid residues;

~~(e)~~(c) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one modification ~~selected from the group consisting of~~ that is a conservative amino acid substitutions, ~~amino acid insertions, amino acid deletions,~~ C-terminal truncation, ~~and~~ or N-terminal truncation, wherein the encoded polypeptide ~~has an activity of~~ is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2 and comprises at least 25 amino acid residues;

~~(f) a nucleotide sequence of any of (a) - (e) comprising a fragment of at least about 16 nucleotides;~~

~~(g)~~(d) a nucleotide sequence ~~which~~ that hybridizes under at least moderately ~~or highly~~ stringent conditions to the complement of the nucleotide sequence of any of (a) - ~~(f)~~(c); ~~and~~ or

~~(h)~~(e) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - ~~(e)~~(d).

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10. (Amended) The process of Claim 8, wherein the nucleic acid molecule comprises promoter DNA other than ~~the promoter DNA for the~~ native IL-1ra-L ~~polypeptide~~ promoter DNA operatively linked to ~~the DNA~~ a nucleic acid molecule encoding ~~the~~ an IL-1ra-L polypeptide.

11. (Amended) The isolated nucleic acid molecule according to Claim 2, wherein the percent identity is determined using a computer program ~~selected from the group consisting of~~ that is GAP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, ~~and~~ or the Smith-Waterman algorithm.

45. (Amended) A nucleic acid molecule encoding a fusion polypeptide comprising the ~~polypeptide~~ nucleic acid molecule of any of Claims ~~13, 14, or 15~~ 1, 2, or 3 fused to DNA encoding a heterologous amino acid sequence.

46. (Amended) The ~~fusion polypeptide~~ nucleic acid molecule of Claim 45, wherein the DNA encoding the heterologous amino acid sequence ~~is~~ encodes an IgG constant domain or biologically active fragment thereof.

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PENDING CLAIMS

Clean Versions of Pending Claims under 37 C.F.R. 1.121(c)(3)

1. An isolated nucleic acid molecule comprising a nucleotide sequence:

(a) as set forth in SEQ ID NO: 1;

(b) of the DNA insert in ATCC Deposit No. PTA-1215;

(c) encoding a polypeptide as set forth in SEQ ID NO: 2;

(d) that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of any of (a) - (c); or

(e) complementary to the nucleotide sequence of any of (a) - (d).

2. An isolated nucleic acid molecule comprising:

(a) a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1215, encoding a polypeptide fragment of at least 25 amino acid residues;

(b) a region of the nucleotide sequence of SEQ ID NO: 1, or the DNA insert in ATCC Deposit No. PTA-1215, comprising a fragment of at least 16 nucleotides;

(c) a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of either (a) or (b); or

(d) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - (c).

3. An isolated nucleic acid molecule comprising:

(a) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2;

(b) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 having a C- and/or N- terminal truncation, wherein the encoded polypeptide comprises at least 25 amino acid residues;

(c) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one modification that is a conservative amino acid substitution, C-terminal truncation, or N-

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terminal truncation, wherein the encoded polypeptide is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2 and comprises at least 25 amino acid residues;

(d) a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of any of (a) - (c); or

(e) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - (d).

4. A vector comprising the nucleic acid molecule of any of Claims 1, 2, or 3.

5. A host cell comprising the vector of Claim 4.

6. The host cell of Claim 5 that is a eukaryotic cell.

7. The host cell of Claim 5 that is a prokaryotic cell.

8. A process of producing an IL-1ra-L polypeptide comprising culturing the host cell of Claim 5 under suitable conditions to express the polypeptide, and optionally isolating the polypeptide from the culture.

10. The process of Claim 8, wherein the nucleic acid molecule comprises promoter DNA other than native IL-1ra-L promoter DNA operatively linked to a nucleic acid molecule encoding an IL-1ra-L polypeptide.

11. The isolated nucleic acid molecule according to Claim 2, wherein the percent identity is determined using a computer program that is GAP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, or the Smith-Waterman algorithm.

42. A composition comprising a nucleic acid molecule of any of Claims 1, 2, or 3 and a pharmaceutically acceptable formulation agent.

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43. The composition of Claim 42, wherein said nucleic acid molecule is contained in a viral vector.

44. A viral vector comprising a nucleic acid molecule of any of Claims 1, 2, or 3.

45. A nucleic acid molecule encoding a fusion polypeptide comprising the nucleic acid molecule of any of Claims 1, 2, or 3 fused to DNA encoding a heterologous amino acid sequence.

46. The nucleic acid molecule of Claim 45, wherein the DNA encoding the heterologous amino acid sequence encodes an IgG constant domain or biologically active fragment thereof.

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